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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,986	05/04/2001	Eyal Raz	UCAL 168	8751

24353 7590 03/15/2004

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EXAMINER	
RILEY, JEZIA	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,986	RAZ ET AL.	
	Examiner	Art Unit	
	Jezia Riley	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 8-12 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 8-12 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: Letter of withdrawal from issue

DETAILED ACTION

1. It is noted that this application has regrettably been withdrawn from issue as stated in the letter enclosed. The following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 8-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Torrance et al. (The Journal of Biological Chemistry, 1998, Vol. 273, pp.20810-20819).

Torrance et al. discloses sequence specific Binding of KU to single stranded DNA. They identified a polypurine/polypyrimidine DNA sequence element (NRE1) within the negative regulatory region of the LTR of the GR strain of MMTV that was sufficient to repress glucocorticoid hormone –induced MMTV transcription. Subsequently, they demonstrated that this sequence functioned as a direct, sequence-specific DNA binding site for KU autoantigen/DNA-dependent protein kinase (DNA-PK). Both Ku and the DNA-PK catalytic subunit (DNA-PKcs) were found to be required for

the transcriptional effects of NRE1 on MMTV expression. Torrance et al. have initiated a characterization of the nuclear factors that bind specifically to the polypurine rich upper strand of NRE1. A singe stranded oligonucleotide affinity column separated NRE1 binding affinity into two fractions. One of the factors was purified to homogeneity. Remarkable, this sequence-specific, single stranded NRE1 binding activity was revealed to be Ku. Further the addition of Mg2+ and/or ATP to a binding reaction containing double stranded NRE1 induced contact of Ku80 with the upper strand of NRE1. In the material and Methods it is shown a nucleic acid sequence comprising a 5'TCG-3' sequence, for example, and labeled at their 5'.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Torrance et al. (The Journal of Biological Chemistry, 1998, Vol. 273, pp.20810-20819) in view of Kelavkar et al. (Genes and immunity 2000, 1, pp. 237-250).

Torrance et al. discloses sequence specific Binding of KU to single stranded DNA. They identified a polypurine/polypyrimidine DNA sequence element (NRE1) within the negative regulatory region of the LTR of the GR strain of MMTV that was sufficient to repress glucocorticoid hormone –induced MMTV transcription. Subsequently, they demonstrated that this sequence functioned as a direct, sequence-specific DNA binding site for KU autoantigen/DNA-dependent protein kinase (DNA-PK). Both Ku and the DNA-PK catalytic subunit (DNA-PKcs) were found to be required for the transcriptional effects of NRE1 on MMTV expression. Torrance et al. have initiated a characterization of the nuclear factors that bind specifically to the polypurine rich upper strand of NRE1. A singe stranded oligonucleotide affinity column separated NRE1 binding affinity into two fractions. One of the factors was purified to homogeneity. Remarkable, this sequence-specific, single stranded NRE1 binding activity was revealed to be Ku. Further the addition of Mg2+ and/or ATP to a binding reaction containing double stranded NRE1 induced contact of Ku80 with the upper strand of

NRE1. In the material and Methods it is shown a nucleic acid sequence comprising a 5'TCG-3' sequence, for example, and labeled at their 5'.

Kelavkar et al. discloses Ku antigen is required for interleukin 13/ 4 induction of lipoxygenase –1 gene expression in human epithelial cells. Experiments using antibodies toward Ku and its individual subunits confirmed that IL-13 and IL –4 activate KU antigens and 15-LO-1 expression in cells. The data suggest that Il-4 and IL 1-13 have specific role in the induction of Ku proteins and that these interleukins possibly regulate protein-protein binding of Ku subunits and hence, their DNA-binding properties- possibly accounting for their unequal potency in the upregulation of 15-LO-1 gene expression.

Therefore it would have been obvious at the time the invention was made to modulate DN-PK activity by measuring an amount of IL-6 or Il-12 produced by the cell since Kelavkar further discloses that the biological significance of Ku expression has also been studied in aging and in cancer. And that a role for Ku80 in autocrine and paracrine IL-6-mediated multiple myeloma cell growth and survival has been demonstrated. That CD40 ligands treatment of multiple myeloma cells with 5E2 mAbs induces a shift of Ku from the cytoplasm to the cell surface. Thus Ku may function as an adhesion molecule that mediates homotypic adhesion of tumor cells, as well as heterotypic adhesion of tumor cells to bone marrow stromal cells and to human

fibronectin. In conclusion the results demonstrates that in human cells Ku appears to play a permissive role in cytokine induction. (Kelavkar page 246).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Wednesday, March 10, 2004

JEZIA RILEY
PRIMARY EXAMINER

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
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MAR 10 2004

In re Application of
RAZ EYAL et al
Serial No: 09/848,986
Filed: 05/04/2001
For: AGENTS THAT MODULATE DNA-PK
ACTIVITY AND METHODS OF USE THEREOF

NOTICE OF WITHDRAWAL FROM ISSUE
UNDER 37 CFR 1.313(c)

The above-identified application is hereby withdrawn from issue after payment of the issue fee to permit reopening of prosecution. See 37 CFR 1.31(c)(2).

The issue fee is refundable upon written request. If, however, the application is again found allowable, the issue fee can be applied toward payment of the issue fee in the amount identified on the new Notice of Allowance and Issue Fee Due upon written request. This request and any balance due must be received on or before the due date noted in the new Notice of Allowance in order to prevent abandonment of the application.

Telephone inquiries should be directed to Gary Benzion at (571) 272-0782

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